Registration Decision RD2016-01

Pyroxasulfone

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Registration Decision for Pyroxasulfone

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is granting full registration for the sale and use of Pyroxasulfone Technical and Pyroxasulfone 85 WG, containing the technical grade active ingredient pyroxasulfone, to control weeds in field corn.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

These products were first proposed for registration in the consultation document[1] Proposed Registration Decision PRD2012-20, *Pyroxasulfone*. This Registration Decision[2] describes this stage of the PMRA's regulatory process for pyroxasulfone and summarizes the Agency's decision, the reasons for it and provides, in Appendix I, a summary of comments received during the consultation process as well as the PMRA's response to these comments. This decision is consistent with the proposed registration decision stated in PRD2012-20, *Pyroxasulfone*.

For more details on the information presented in this Registration Decision, please refer to the Proposed Registration Decision PRD2012-20, *Pyroxasulfone* that contains a detailed evaluation of the information submitted in support of this registration.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[3] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its conditions of registration. The Act also requires that products have value[4] when used according to label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

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1 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

3 "Acceptable risks" as defined by subsection 2(2) of *Pest Control Products Act*.

4 "Value" as defined by subsection 2(1) of *Pest Control Products Act* "... the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact".

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment. These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

What Is Pyroxasulfone?

Pyroxasulfone is a novel pre-emergence herbicide discovered amongst a series of herbicidal 3-sulfonylisoxazoline derivatives. Pyroxasulfone inhibits very-long-chain fatty acid (VLCFA) synthesis by interfering with elongation of the C18 chains, which are normally catalyzed by VLCFA elongases. This causes inhibition of shoot elongation after seed germination. Formation of cell membranes and waxy cuticle materials within developing plant tissue is also severely affected by lack of VLCFAs. The active ingredient, pyroxasulfone, enters target plants through root-uptake or via the apical meristem. This compound is primarily efficacious against annual grasses and also provides control of certain broadleaf weeds.

Pyroxasulfone is regarded as a Weed Science Society of America Group 15 Herbicide or Herbicide Resistance Action Committee Group K3 Herbicide.

Health Considerations

Can Approved Uses of Pyroxasulfone Affect Human Health?

Pyroxasulfone is unlikely to affect your health when used according to label directions.

Potential exposure to pyroxasulfone may occur through the diet (food and water) or when handling and applying the product. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when pyroxasulfone products are used according to label directions.

Pyroxasulfone was of low acute toxicity by the oral, dermal and inhalation routes of exposure. It was minimally irritating to the eyes and non-irritating to the skin. Pyroxasulfone was not considered to be a skin sensitizer. Consequently, no hazard signal words are required on the label.

The end-use product Pyroxasulfone 85 WG was of low acute toxicity via the oral, dermal and inhalation routes of exposure in rats, and was minimally irritating to the skin and eyes of rabbits. It was a skin sensitizer in guinea pigs. Consequently, the hazard signal words "POTENTIAL SKIN SENSITIZER" are required on the label.

Based on the weight of evidence, pyroxasulfone did not cause damage to genetic material. There was no indication that it causes birth defects in the developing young, or effects on the immune or reproductive systems. The target organs of toxicity following pyroxasulfone treatment included the liver, heart, kidney, skeletal muscle and peripheral nerves. Pyroxasulfone caused urinary bladder tumours in male rats at a high dose level. There was evidence that pyroxasulfone caused damage to the nervous system. When pyroxasulfone was given to pregnant or nursing animals, effects of a serious nature (changes in brain development) were observed on both the developing fetus and juvenile animal at doses that were not toxic to the mother, indicating that the young were more sensitive to pyroxasulfone than the adult animal. The risk assessment takes this sensitivity into account in determining the allowable level of human exposure to pyroxasulfone, and protects against the noted adverse effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

Residues in Water and Food

Dietary risks from food and water are not of concern.

Aggregate dietary intake estimates (food plus water) revealed that the general population and all infants (<1 year), the subpopulation which would ingest the most pyroxasulfone relative to body weight, are expected to be exposed to less than 93% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from pyroxasulfone is not of concern for all population sub-groups. There are no cancer risks of concern.

An aggregate (food and water) dietary intake estimate for the highest exposed population (all infants, <1 year old) used less than 54% (95th Percentile) of the acute reference dose, which is not a health concern.

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Food containing a pesticide residue at the established MRL does not pose an unacceptable health risk.

Residue trials conducted throughout the United States using pyroxasulfone on field corn are acceptable.

Occupational Risks From Handling Pyroxasulfone 85 WG

Occupational risks are not of concern when Pyroxasulfone 85 WG is used according to the proposed label directions, which include protective measures.

Farmers and custom applicators who mix, load or apply Pyroxasulfone 85 WG as well as field workers re-entering freshly treated fields can come in direct contact with pyroxasulfone residues on the skin. Mixers, loaders and applicators may also be exposed by breathing sprays and mists. Therefore, the label specifies that anyone mixing/loading and applying 41 kg or less of Pyroxasulfone 85 WG must wear a long-sleeved shirt, long pants and chemical-resistant gloves. Anyone mixing/loading more than 41 kg of Pyroxasulfone 85 WG must wear chemical-resistant coveralls over a long-sleeved shirt and long pants, and chemical-resistant gloves. Anyone applying more than 41 kg of Pyroxasulfone 85 WG must wear coveralls over a long-sleeved shirt and long pants and must apply in a closed cab tractor.

The label also requires that workers do not enter treated fields for 12 hours after application. Taking into consideration these label statements, the number of applications and the expectation of the exposure period for handlers and workers, the risk to these individuals is not a concern. There are no cancer risks of concern.

For bystanders, exposure is expected to be much less than that for workers and is considered negligible. Therefore, health risks to bystanders are not of concern.

Environmental Considerations

What Happens When Pyroxasulfone Is Introduced Into the Environment?

Pyroxasulfone will enter the environment when applied once a year to field corn. Pyroxasulfone will dissipate in the environment primarily through leaching and gradual biotransformation to the major transformation product KIH-485-M-1. The risk to aquatic organisms can be mitigated with buffer zones.

Pyroxasulfone has low solubility and volatility. It is not expected to transform through hydrolysis or phototransformation. Pyroxasulfone and its major transformation product, KIH-485-M-1, are not expected to transform quickly in the terrestrial or aquatic environment through microbially mediated processes. In the aquatic environment, pyroxasulfone has a tendency to partition to the sediments where it gradually transforms into KIH-485-M-1, which re-solubilises to the water column and gradually accumulates. Pyroxasulfone and its major transformation product are considered to be persistent to moderately persistent in terrestrial and aquatic environments.

Pyroxasulfone and its major transformation product, KIH-485-M-1, do not adsorb strongly to soil particles and are expected to have high mobility in soil. Pyroxasulfone and KIH-485-M-1 are expected to dissipate quickly from the soil surface in the field. The major route of dissipation in the environment for pyroxasulfone and its major transformation product is expected to be leaching to ground water.

When applied using a ground boom sprayer, there is a potential for exposure of non-target organisms in the environment to pyroxasulfone and its major transformation product as a result of runoff and spray drift. Pyroxasulfone and its major transformation product, KIH-485-M-1, were practically non-toxic to most non-target organisms. Pyroxasulfone is highly toxic to aquatic plants, especially freshwater algae. The risk to these aquatic non-target organisms can be mitigated with buffer zones.

Value Considerations

Pyroxasulfone, as a pre-plant surface, pre-emergence treatment or an early post-emergence treatment on field corn, provides control of annual grasses and certain broadleaf weeds.

A single application of pyroxasulfone provides effective residual control of annual grasses, including barnyard grass, giant foxtail, yellow foxtail, green foxtail, Italian ryegrass, large crabgrass, and redroot pigweed and common waterhemp in all types of field corn in Canada.

Pyroxasulfone is compatible with integrated weed management practices in conservation and conventional crop cultivation systems.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures being proposed on the label of Pyroxasulfone 85 WG to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

Because there is a concern with users coming into direct contact with pyroxasulfone residues on the skin or through inhalation of spray mists, anyone mixing/loading and applying 41 kg or less of Pyroxasulfone 85 WG must wear a long-sleeved shirt, long pants and chemical-resistant gloves. Anyone mixing/loading more than 41 kg of Pyroxasulfone 85 WG must wear chemical-resistant coveralls over a long-sleeved shirt and long pants, and chemical-resistant gloves. Anyone applying more than 41 kg of Pyroxasulfone 85 WG must wear coveralls over a long-sleeved shirt and long pants and must apply in a closed cab tractor.

The label also requires that workers do not enter treated fields for 12 hours after application. In addition, standard label statements to protect against drift during application were added to the label.

Environment

Based on the risk identified to off-target sensitive habitats, buffer zones of 1 to 5 m are required to protect terrestrial and freshwater habitats, respectively.

Other Information

The relevant test data on which the decision is based (as referenced in PRD2012-20, *Pyroxasulfone)* are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra.infoserv@hc-sc.gc.ca).

Any person may file a notice of objection[5] regarding this registration decision within 60 days from the date of publication of this Registration Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the Pesticides and Pest Management portion of the Health Canada's website (Request a Reconsideration of Decision) or contact the PMRA's Pest Management Information.

[5] As per subsection 35(1) of the *Pest Control Products Act*.

Appendix I Comments and Responses

Comment on potential impact of pesticides on honey bees.

A comment was received which expressed a concern about the adverse impact of pesticide use may have on honey bees.

Response

PMRA has reviewed the comment received and determined that while this comment does not specifically refer to the Proposed Registration Decision PRD2012-20, *Pyroxasulfone*, PMRA does take the impact of pesticides in general and, in this case Pyroxasulfone specifically, on pollinators, for example, honey bees very seriously.

Prior to registration, pesticide products must undergo rigorous human health and environmental risk assessments and are registered for sale and use in Canada only if stringent safety standards are met. As part of this process a variety of environmental toxicity studies including toxicity to birds, bees and aquatic organisms are examined in detail. Environmental toxicity information is considered in combination with the environmental fate of the chemical (i.e. consideration is made to the potential of the chemical to reach surface water, groundwater, air and food in order to determine the risk posed to various organism groups). If the specified use of a product poses risks of concern to the environment, it is not registered for use in Canada.

In addition to the initial risk assessment conducted upon registration of a product, PMRA has several post-marketing strategies in place to assess whether pesticides continue to meet our environmental standards. These include the pesticide Incident Reporting Program and a re-evaluation program where pesticides are re-evaluated every fifteen years using the latest scientific methods and information, information in the scientific literature, and assessments conducted by other regulatory authorities, to determine if changes to the registration of the pest control product are required.

PMRA will continue to ensure that only pest control products meeting our stringent health and environmental standards are approved for use in Canada.

The PMRA is aware of the importance of bees and the beekeeping industry to the production of food in Canada, as well as the issues regarding bee health, including concerns about potential chronic effects of pesticides. PMRA scientists are working with scientists from universities and other organizations (for example, Agriculture and Agri-Food Canada, provincial ministries of Agriculture and Environment, the Canadian Association of Professional Apiculturists and other regulatory agencies in the United States and Europe) to determine whether pesticides are contributing to pollinator declines.

PMRA applies a science-based approach to regulate pesticides. PMRA will continue to closely monitor scientific information and other developments related to potential impacts of pest control products on pollinators, not only in Canada and the United States, but also in Europe. PMRA will consider further action if appropriate.

In reference to pyroxasulfone, based on the detailed review of appropriate data, this active ingredient is considered relatively non-toxic to bees (LD_{50} >100 µg/bee, equivalent to 112 kg a.i./ha), which is the lowest toxicity classification for bees. As such, the residues in pollen or nectar would not be sufficient to cause any effects to bees. No effects were noted up to the tested dose of 100 µg/bee.

Further details on the potential risk to honey bees and birds from exposure to pyroxasulfone are provided in Proposed Registration Decision PRD2012-20, *Pyroxasulfone*.